Amendments to the Claims:

1. (Original) An isolated Apo-2 ligand variant polypeptide comprising an amino acid sequence which differs from the native sequence Apo-2 ligand polypeptide sequence of Figure 1 (SEQ ID NO:1) and has one or more of the following amino acid substitutions at the residue position(s) in Figure 1 (SEQ ID NO:1): S96C; S101C; S111C; R170C; K179C.

2. (Original) An isolated Apo-2 ligand variant polypeptide comprising one or more amino acid mutations in the amino acid sequence of native Apo-2 ligand polypeptide sequence of Figure 1 (SEQ ID NO:1), said mutations comprising one or more amino acid substitutions recited in Table II.

Claim 3 (Cancelled).

4. (Original) The Apo-2 ligand variant polypeptide of claim 2 wherein said Apo-2 ligand variant polypeptide induces apoptosis in at least one type of mammalian cell.

5. (Original) The Apo-2 ligand variant polypeptide of claim 4 wherein said mammalian cell is a cancer cell.

Claim 6 (Cancelled).

7. (Original) The Apo-2 ligand variant polypeptide of claim 2 wherein said one or more amino acid mutations comprises one or more amino acid substitutions at positions 189, 193, 199, or 201 of the native Apo-2 ligand sequence.

8. (Original) The Apo-2 ligand variant polypeptide of claim 2 wherein said Apo-2 ligand variant polypeptide retains native residues at positions corresponding to Arg149, Gln205, Val207, Tyr216, Glu236 and/or Tyr237.

9. (Original) An isolated Apo-2 ligand variant polypeptide comprising an amino acid sequence which differs from the native sequence Apo-2 ligand polypeptide sequence of Figure 1 (SEQ ID NO:1) and has a set of amino acid substitutions at the residue position(s) in Figure 1 (SEQ ID NO:1) selected from the group consisting of:
Y189A:R191K:Q193K,
Y189A:R191K:Q193K:H264A,
Y189Q:R191K:Q193R:H264R:I266L:D267Q,
Y189A:R191K:Q193K:H264D:I266L:D267Q:D269E, and
Y189A:R191K:Q193R:H264S:I266L:D269E.

10. (Original) An isolated Apo-2 ligand variant polypeptide comprising one or more amino acid mutations in the amino acid sequence of native Apo-2 ligand polypeptide sequence of Figure 1 (SEQ ID NO:1), said mutations comprising one or more amino acid substitutions recited in Table III.

11. (Original) The Apo-2 ligand variant polypeptide of claim 10 wherein said Apo-2 ligand variant polypeptide has selective binding affinity for DR5 receptor.

12. (Original) The Apo-2 ligand variant polypeptide of claim 10 wherein said Apo-2 ligand variant polypeptide induces apoptosis in at least one type of mammalian cell.

13. (Original) The Apo-2 ligand variant polypeptide of claim 12 wherein said mammalian cell is a cancer cell.

14. (Original) The Apo-2 ligand variant polypeptide of claim 11 wherein said DR5 receptor comprises amino acids 1 to 184 of Fig. 3A (SEQ ID NO:4).

15. (Original) The Apo-2 ligand variant polypeptide of claim 10 wherein said one or more amino acid mutations comprises one or more

amino acid substitutions at positions 189, 191, 193, 264, 266, 267, or 269 of the native Apo-2 ligand sequence.

16. (Original) The Apo-2 ligand variant polypeptide of claim 10 wherein said Apo-2 ligand variant polypeptide retains native residues at positions corresponding to Arg149, Gln205, Val207, Tyr216, Glu236 and/or Tyr237.

17. (Original) An isolated Apo-2 ligand variant polypeptide comprising one or more amino acid mutations in the amino acid sequence of native Apo-2 ligand polypeptide sequence of Figure 1 (SEQ ID NO:1), said mutations comprising one or more amino acid substitutions recited in Table VII.

18. (Original) The Apo-2 ligand variant polypeptide of claim 17 wherein said Apo-2 ligand variant polypeptide has selective binding affinity for DR5 receptor.

19. (Original) The Apo-2 ligand variant polypeptide of claim 17 wherein said Apo-2 ligand variant polypeptide induces apoptosis in at least one type of mammalian cell.

20. (Original) The Apo-2 ligand variant polypeptide of claim 19 wherein said mammalian cell is a cancer cell.

21. (Original) The Apo-2 ligand variant polypeptide of claim 18 wherein said DR5 receptor comprises amino acids 1 to 184 of Fig. 3A (SEQ ID NO:4).

22. (Original) An isolated Apo-2 ligand variant polypeptide comprising an amino acid sequence which differs from the native sequence Apo-2 ligand polypeptide sequence of Figure 1 (SEQ ID NO:1) and has a set of amino acid substitutions at the residue position(s) in Figure 1 (SEQ ID NO:1) selected from the group consisting of:
Y189Q:R191K:Q193R; H264R; I266L; D267Q;

Y189Q:R191K:Q193R; and
Y189Q:R191K:Q193R:I266L.

23. (Currently Amended) The Apo-2 ligand variant polypeptide of any of claims 1-~~22~~ 2, 4, 5, and 7-22 wherein said polypeptide is conjugated or linked to one or more polyols.

24. (Original) The Apo-2 ligand variant polypeptide of claim 23 wherein said polyol is polyethylene glycol.

25. (Original) The Apo-2 ligand variant polypeptide of claim 24 wherein said polyethylene glycol has an average molecular weight of about 1000 daltons to about 25,000 daltons.

26. (Currently Amended) An isolated nucleic acid molecule comprising DNA encoding the Apo-2 ligand variant polypeptide of any of claims 1-~~22~~ , 2, 4, 5, and 7-22.

27. (Original) A vector comprising the encoding DNA of claim 26.

28. (Original) A host cell comprising the vector of claim 27.

29. (Original) The host cell of claim 28 wherein said host cell is an E. coli cell, CHO cell or yeast cell.

30. (Original) A method of producing Apo-2 ligand variant polypeptide comprising culturing the host cell of claim 28 under conditions sufficient to express said Apo-2 ligand variant polypeptide and recovering said Apo-2 ligand variant polypeptide from said culture.

31. (Currently Amended) A composition comprising the Apo-2 ligand variant polyeptide of any of claims 1-~~25~~ , 2, 4, 5, and 7-22.

32. (Original) The composition of claim 31 wherein said composition comprises a therapeutically acceptable formulation which contains one or more divalent metal ions.

33. (Currently Amended) A method of inducing apoptosis in mammalian cells comprising exposing mammalian cells expressing ~~DR4 and/or~~ DR5 receptor or both DR4 and DR5 receptor to an effective amount of Apo-2 ligand variant polypeptide of any of claims 1~~-25~~ , 2, 4, 5, and 7-22.

Claims 34-38 (Cancelled).